Job No.: 6234-89423 Ref.: 17509-0001
Translated from German by the Ralph McElroy Translation Co.
910 West Avenue, Austin, Texas, 78701

INTERNATIONAL PATENT OFFICE
WORLD ORGANIZATION FOR INTELLECTUAL PROPERTY
International patent published on
the basis of the Patent Cooperation Treaty
INTERNATIONAL PUBLICATION NO. WO 02/056862 A2

International Patent Classification[7]:	A 61 K 9/00
International Filing No.:	PCT/DE01/04874
International Filing Date:	December 20, 2001
International Publication Date:	July 25, 2002
Priority	
Date:	December 20, 2000
Country:	DE
No.:	100 63 612.8
Filing Language:	German
Language of Publication:	German

MICROSYSTEM FOR CONTROLLED DISPENSATION OF AN ACTIVE SUBSTANCE FROM A RESERVOIR

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Designated States (national): CN, JP, US

Designated States (regional): European Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR).

Published
- Without International Search Report, must be republished after the report is received.

For an explanation of the two-letter codes and the other abbreviations, please refer to the explanations ("Reference Notes on Codes and Abbreviations") at the beginning of each regular edition of the PCT Bulletin.

Abstract: The invention relates to a microsystem for controlling the release of an active substance from a reservoir, comprising a thin carrier substrate (1) which is made of a material which is impermeable with respect to the active substance and has one or more through openings (5) for the active substance. Several electrodes (3) are arranged in the region of the through openings (5) and can be controlled by means of an electronic system (2) which is integrated into the carrier substrate (1). The through openings (5) are embodied in the form of microgaps and/or microchannels respectively comprising electrodes (3) on both sides and covered by a layer (7) of an electroporous material on one side of the carrier substrate. The microsystem can be used advantageously for controlled release of an active substance in applications where space requirements are critical.

Technical application field

The present invention relates to a microsystem for controlling the dispensation or release of an active substance from an active substance reservoir, with a thin carrier substrate which consists of a material which is impermeable with respect to the active substance and which presents one or more through openings for the active substance, several electrodes arranged in the area of the through openings, as well as an electronic system integrated in the carrier substrate for controlling the electrodes. The invention, moreover, relates to medical implants with such a microsystem.

The controlled or managed local in vivo release of active substances in the body of a patient is of great significance in the treatment of diseases and in reducing side effects when using implants. Medical implants frequently cause adverse reactions such as, for example, infections in the human body, which can be caused by damage to the epithelium, by encouraging growth of microorganisms, or by influencing the immune system or by contaminated implants. The risk of adverse reactions of the body can be minimized by the incorporation of miniaturized devices in the implants which release, for example, appropriate active substances to prevent infections. There is also a demand for controlled local release of drugs in the treatment of certain diseases, for example, in tumor control.

Microsystems, such as that of the present invention, are particularly suitable because of their small dimensions for use in the local and controlled release of an active substance in human bodies.

State of the art

The controlled release of active substance in the human body over a certain time period is currently carried out using different systems. It is known to incorporate active substances in a polymer, from which they diffuse over a certain period of time. Furthermore, polymers can be used which effect a controlled degradation, over a predetermined time period, of active substances in the body. With the aid of these systems, the active substance concentration can be maintained in the desired therapeutic range using only one dose. In implantations, the systems make it possible to restrict the release of active substances to certain body parts, so that the required quantity of systemic drugs is reduced, and the degradation of larger quantities of active substance by the body is prevented.

A review of the known systems for the controlled release of active substances is given, for example, in the article by J. M. Schierholz et al., "Sophisticated Medical Devices as Local Drug-Delivery Systems," Med. Device Technol. 11, 12-17 (2000).

However, a multitude of clinical situations exist where the release, at a constant rate over time, of active substances is no longer sufficient. Examples of such situations are the release of insulin in patients with diabetes mellitus, antierythema agents in patients with heart rhythm disorders, gastric acid inhibitors to treat tumors, nitrides for patients with angina pectoris, as well as the use of selective β-receptor blockers, for birth control, for hormone replacement, for immunization and for cancer therapy. In such applications, the course over time of the release of the active substance must be such that it can be adjusted in a targeted manner to the physiological requirements.

To improve the control of the release of active substance, in particular to carry out a release which can be actively controlled, polymers have been developed which can be controlled by external influences, such as ultrasound, electric or magnetic fields, light, enzymes, pH and temperature changes for the controlled release of the active substances incorporated therein. A review of such systems is given, for example, in the article by J. Kost et al., "Responsive Polymer Systems for Controlled Delivery of Therapeutics," Trends Biotechnol. 10, 127-131 (1992).

A widespread drawback of these polymer-based systems, however, consists of their partially deficient biocompatibility and undesired toxicity, relatively slow reaction time to stimuli, limited lifespan, as well as the fact that, in many cases, the reproducibility of the active

substance decrease is insufficient. Furthermore, the delivery of quantities of active substance, which are of relevance in practice, is made difficult because of the limited uptake capacity of the polymers.

In US 4,003,779, US 4,146,029, US 3,692,027 and US 4,360,019, microsystems for the controlled release of active substances are described which use mechanical systems, in particular miniaturized, electrically driven components for the release of active substance from a reservoir. It is precisely the reliability of the release of active substance in the case of small quantities which still presents problems in such mechanical systems.

An additional mechanism for the controlled release of active substances from an active substance reservoir is described in US 5,556,528. This patent uses a microsystem in the form of a nanoporous membrane made, for example, of P2VB, onto which an active control structure in the form of a thin layer made of molecules with a dipole moment larger than 5 debye has been applied. This thin control layer has the property that its permeability with respect to the active substances to be released changes as a function of the electrical field strength which works in the opposite direction. This effect, which is known as electroporation in the field of cell research, makes it possible to render the control layer permeable or impermeable with respect to the active substances by means of an electrical control. The underlying principle can be obtained, for example, from the publication by P. F. Lurquin, "Gene Transfer by Electroporation," Mol. Biotechnol. 7, 5-35 (1997).

A concrete embodiment of the functional microsystem for use in the human body based on the principle of electroporation cannot, however, be obtained from US 5,556,528.

US 5,797,898 describes a microsystem made of a planar microchip in which cavities are etched as active substance reservoirs. The active substance reservoirs are closed with reservoir caps, which are made of electrically conducting layers and which undergo electrochemical decomposition when an electric potential is applied to them. The microchip disclosed as an embodiment example has a thickness of 300 µm and contains several active substance reservoirs having opening surfaces of 30 x 30 µm, which are arranged in an array pattern. An electronic system is incorporated in the microchip for controlling the electrically conducting layers, which are formed as electrodes, to close the microreservoir. Such a microsystem can be implemented with known techniques of semiconductor technology.

By controlling the corresponding electrodes, the electrically conducting reservoir caps can be caused to decompose, in a targeted manner, so that the active substance located under it, in the active substance reservoir, can be released. However, it is not possible to carry out a repeated controlled release of active substance from a single reservoir using this technique. To achieve that purpose, a multitude of different reservoirs must be provided, which can then be

opened in succession, in accordance with the desired release of active substance. An additional drawback of these microsystems consists in that the material of the reservoir caps, during the decomposition, is released into the physiological environment. Because of the multitude of reservoirs which are required for repeated controlled release of active substance, and because of the relatively rigid structure of this microsystem, its utilization encounters problems when carried out in situations where there are critical space requirements, for example, in connection with small prostheses or in certain body regions, such as the brain.

The obejctive of the present invention consists in providing a microsystem, as well as the design of an implant with a microsystem, which allow an event-controlled in vivo release of active substances, even in applications with very critical space requirements.

Presentation of the invention

The problem is solved with the microsystem and the implant according to Patent Claim 1 or 21. Advantageous embodiments of the microsystem as well as of the implant constitute the object of the subclaims.

The present microsystem consists of a thin, mechanically flexible carrier substrate which consists of a material which is impermeable with respect to the active substance and which presents one or more through openings for the active substances. The through openings are designed as microchannels and/or microgaps and they are covered on one side of the carrier substrate with a layer which is made of an electroporous material. On both sides of the microchannels and/or microgaps, electrodes are formed which can be controlled by an electronic system which is incorporated in the carrier substrate.

The electroporous material consists advantageously of a lipid film, in which pores can be reversibly generated by the application of an electrical field, which pores are permeable with respect to the active substances to be released. The microchannels and/or microgaps have dimensions which are such that they allow, on the one hand, the passage of the active substances, and, on the other hand, an overlapping with a cohesive lipid film. It is preferred for these microgaps or microchannels to have an opening width of at most 10 µm.

The carrier substrate preferably consists of a diluted silicon substrate, into which the microgaps and/or microchannels have been etched. To achieve a sufficient flexibility of this carrier substrate, the thickness achieved in the end is less than approximately 80 µm. Here the electrodes are preferably applied in the form of thin electrode areas onto the carrier substrate or integrated in its surface, where the layer which is made of electroporous material is applied onto these electrodes, or areas thereof. Such a construction can be carried out with known techniques of semiconductor technology, in a simple manner.

The present microsystem, which is referred to as a film system below, because of its small thickness and a high flexibility, is applied onto active substance reservoirs, which can be incorporated, for example, in prostheses, in such a manner that the film structure seals the active substances from the physiological environment. Besides the active substance reservoir which is integrated in the implants, such reservoirs can naturally also be applied in the form of a solid layer to the film system.

Through the electrodes, and with the electronic system which is integrated in the system, it is possible to apply an electrical field to the layer made of electroporous material, which field reversibly generates pores in those areas of the layer in which there are microgaps. As a function of the temporal variation of the field strength versus time, and the type of electroporous material, the pores either have a limited lifespan or they are permanent. As long as the pores are generated, active substances are released from the reservoirs through the pores into the physiological environment. When the electrical fields are switched off, the pores close, and the release of active substance is interrupted.

The control of the electric potential which is applied to the electrodes by the electronic system can be triggered by different components. In one embodiment this purpose can be fulfilled by a biosensor can be which generates the trigger signal as a function of the concentration of certain active substances in the environment. Furthermore, the control signals can be transmitted to the electronic system via telemetry or using appropriate software with a predetermined program course, where the software can be provided in a program storage device integrated in the carrier substrate. The biosensor, as well as connections for trigger signals, can be directly attached to the microsystem or integrated in it.

The power supply for the electronic system can be achieved, for example, by a wireless method using an inductive process with a transmission coil which is external to the body. The receiving coil can be integrated in the film system, or it can be designed as a separate unit. To ensure a continuous power supply and to make available the energy required for the generation of the electrical fields above the electroporous layer, an energy storage device can also be provided on the film system. For example, this energy storage device can be continuously charged via appropriate coils by induction from the exterior, so that it can deliver the entire output in the case of energy consumption over a short period of time.

Because of its flexible design, the present microsystem design can be adapted in a flexible manner to the shape of prostheses and to the physiological space requirements in the body, so that it needs only a minimum amount of space. It can readily be combined with prostheses without negative effect on their function. Naturally, the microsystem can also be inserted, appropriately equipped with an active substance reservoir, separately, for example, in

the blood stream. As a result of its flexible design, it can be optimally adapted to a given environment in the process.

The microsystem is particularly advantageous for applications in connection with small prostheses, such as, for example, stents which are inserted into vessels of the blood stream, cardiac arteries or the airways. It is precisely in such applications that the known systems of the state of the art present problems because of the space requirement, which cannot be ignored.

The electrodes can be controlled by an electronic system which is triggered by physiological events. Therefore, active substance can be released as a function of the possible physiological requirements. An erroneous triggering due to external electrical or magnetic fields can be ruled out. As a result of a reversible design of the pores in the electroporous layer, in particular in a lipid membrane, the controlled release of active substance can be carried out repeatedly from a single reservoir. The materials which cover the active substance reservoirs in the present microsystem are not released into the physiological environment during the release of active substance.

In a particularly advantageous embodiment, the layer made of electroporous material is located between substrates with corresponding microgaps or microchannels whose openings are located above each other, so that the microgaps or microchannels of one substrate in each case form a single flow channel with the microgaps or microchannels of the other substrate, whose flow can be controlled via the layer made of electroporous material. This arrangement has the advantage of providing improved protection for the layer made of electroporous material. Furthermore, such an arrangement can be attached in a simple manner to a prothesis, that is without taking into account the layer made of electroporous material. The electrodes can be applied, in the same manner as in the case of a simple carrier substrate, to the substrate or integrated in its surface. Here, electrodes can be provided in both substrates or in only one of the two substrates. Such an alternate arrangement is conceivable, for example, one electrode on one side of the microgap in one substrate and the other electrode on the other side of the microgap in the other substrate. For the arrangement of the electrodes, according to the present invention, it is only required that a sufficiently strong electrical field can be applied, through these electrodes, to the electroporous material in the area of the microchannels or microgaps to be able to allow the release of active substance by pore formation. The exact arrangement of the electrodes for achieving this effect is not essential for the present invention and it is left up to the discretion of the person skilled in the art.

Such an arrangement consisting of a layer made of electroporous material, and located between two carrier substrates, can be very advantageously achieved by manufacturing an appropriately larger substrate with twice the surface area of the individual substrates, by

machining it to produce the microchannels, electrodes, electronic system and electroporous layers, and then by folding it together.

The carrier substrate does not necessarily have to consist of a silicon chip. For example, it can also be formed of a polyimide film, in which a thin silicon chip hybrid is integrated.

To increase the compatibility of the carrier substrate with the physiological environment, the latter substrate can be coated with the biocompatible material on the surface which comes in contact with this environment.

In a variant of the microsystem, the surface of the carrier substrate which is opposite the electroporous layer and which comes in contact with the physiological environment, as well as the internal walls of the through openings are designed in a special manner. The surfaces of the opening areas and of the internal walls of the opening are here designed in such a manner that cell adhesion to the surface is prevented. The surface between the opening is designed in such a manner that the cells can adhere. As a result, one prevents, on the one hand, the growth of cells into the openings and thus damage to the lipomembrane, and one achieves, on the other hand, a fixation of the system. The surface modification can be carried out by nanostructuring and/or coating with an appropriate material.

The present microsystem can be used to great advantage in combination with an implant into which the active substance reservoir is incorporated. The microsystem is here fixed in such a manner to the implant, in particular glued to it, that the microgaps and/or microchannels in each case are located above the active substance reservoir. Furthermore, the individual areas between the active substance reservoirs are additionally sealed off by the microsystem. By the integration of the active substance reservoirs in the implant it is thus possible to achieve an arrangement, which is highly space saving, for release of active substance because the present microsystem can be flexibly adapted to the surface of the implant and it presents only a very small thickness.

Naturally, the active substance reservoirs can also be fixed, in the form of a solid phase, to the implant, to which the present microsystem is then applied.

The present microsystem as well as the implant with such a microsystem are again described briefly below with reference to embodiment examples in connection with the figures, without, however, limiting the general inventive idea. In the drawings:

Figure 1 shows a schematic cross-sectional representation of a flexible microsystem on a prosthesis according to an embodiment of the present invention;

Figure 2 shows an example of the electrode control, in the form of a schematic, which is implemented in the microsystem;

Figure 3 shows an example of the microsystem for controlled release of active substance, in a cross-sectional representation (a) as well as in a layout (b);

Figure 4 shows an example of the microsystem in combination with active substance reservoirs;

Figure 5 shows an example of a microsystem according to an additional variant of the present invention with enclosed lipid film, in a schematic cross-sectional representation (a) as well as in an electrode layout (b);

Figure 6 shows an additional example of a microsystem according to the present invention with enclosed lipid film, in schematic cross-sectional representation (a) as well as in an electrode layout (b); and

Figure 7 shows two examples of a microsystem according to the invention with embedded lipid layer in combination with active substance reservoirs.

Procedures for carrying out the invention

For the manufacture of a film microsystem like the one of the present invention, a silicon wafer is used as the starting material in this example. Individual chips 1 with integrated circuit 2, electrode structures 3 for the generation of electrical fields, insulated metal tracks 4 for constructing the receiver coil and connection pads are manufactured on the wafer, using standard semiconductor technology. A corresponding layout can be seen, for example, in Figure 3b. After the application of these structures, the wafer thickness is reduced by etching of the back side to approximately 10 µm. To guarantee a high reliability of the electronic circuit, the areas in which the active circuits 2 are located are only thinned to 80 µm.

Then, on the top side of the wafer, an etching mask is prepared by photolithography, and the microgap 5 is produced by reactive ionic etching. This microgap 5 has the dimensions 100 µm x 1 µm in the present example.

From Figure 3b it can be seen that the electrodes 3 in each case are arranged on both sides of the microgap 5. The microgaps 5 themselves are distributed in an array pattern at fixed intervals to each other on the carrier 1.

As energy storage device, in the present example, SMD capacitors 6 are connected by soldering to the connection surfaces which are provided for that purpose on the chips 1. To ensure the biostability and the biocompatibility of the applied structures, the back side of the wafer, which comes in direct contact with the physiological environment, is coated with parylene by gas phase deposition.

The application of the electroporous layer 7 made of oxidized cholesterol is carried out after separation of the wafer into individual chips. The coating with the electroporous material is carried out selectively in each case above the corresponding microgaps 5. For this purpose, the bottom of a dish, which is provided with one or more corresponding openings, is adjusted with

respect to the chip surface and at the corresponding places; that is, above the microgaps, they are pressed onto the chip surface. Then, dissolved oxidized cholesterol is introduced into the dish. The solvent is evaporated by means of a nitrogen flow so that a film 7 made of oxidized cholesterol forms on the exposed areas of the chip surface, which are exposed as a result of the openings in the dish. As a result of the small opening width of the microgap, the latter are completely covered by this film 7.

The flexible microsystem which has been produced in this manner can then be glued by the top side, that is the side with the film 7 made of oxidized cholesterol, to the reservoir filled with the active substance.

Figure 3a shows a cross section of a microsystem manufactured in this manner. In the cross section, one can see the electrodes 3 on both sides of the microchannels 5, the carrier substrate 1, the layer 7 made of oxidized cholesterol, and a chip adhesive 8 for the attachment of the microsystem to the active substance reservoir. By controlling the film 7 made of oxidized cholesterol via the electrodes 3, which in each case are arranged on both sides, it is possible to make the microgap 5 permeable with respect to the active substances, so that a controlled release of active substance can be affected by this control. Both the trigger signals for controlling the integrated circuit 2 as well as the energy supply to charge the capacitor 6 can be achieved through the integrated coil 4 from outside the body, into which such a microsystem has been introduced.

Figure 1 shows a schematic cross-sectional representation of a flexible film microsystem like that of Figure 3 for the controlled release of active substance in a prosthesis 9. In the present example, active substance reservoirs 10 are incorporated in the prosthesis 9, in which the active substance is located. The microsystem, in this example, is glued to the internal side of this prosthesis 9 to seal, in this manner, the active substance reservoirs from each other and from the environment by means of the adhesive 8. By controlling the electroporous layer 7 via the electrodes 3, the microgaps 5 are released for the active substance, so that the latter can be released from the active substance reservoir 10 into the environment. The electronic system 2 which is integrated in the flexible carrier substrate 1 is not shown in this drawing.

Figure 2 shows, as an example, a schematic for the electrode control which can be carried out in the present microsystem. The control itself is located in the integrated circuit 2. Via that circuit, the desired potential, or a potential having a certain variation over time, is applied to the electrodes 3. A triggering of the integrated circuit 2 from outside can be carried out via a biosensor, a program storage device or a connection 11 for a trigger signal. Furthermore, the integrated circuit 2 is connected to a power source 12 as well as to an energy storage 13 or a

connection for the energy storage. The energy or power supply can be carried out by means of an appropriate reception coil, as already explained above.

Figure 4 shows an example where a microsystem such as the one of Figure 3 is applied to a carrier 15 with active substance reservoirs. The connection between the microsystem and the carrier 15 can be made, for example, by means of a chip adhesive 8, which simultaneously effects the sealing of the system from the exterior.

In a cutout of this microsystem, shown in the figure, one can also see areas 17 on the surface of the carrier substrate 1 which favor adhesion of cells, as well as areas 18, provided only to prevent adhesion. As a result of this surface design, one prevents, on the one hand, the cells from growing into the opening 5, and thus one prevents damage to the lipid membrane, and, on the other hand, one achieves a fixation of the system in the body attachment by growth of the cells in the areas 17.

Figures 5-7 show, as examples, embodiments of a microsystem in which a lipid film 7 is enclosed between two substrates 1,14. Both substrates 1 and 14 are designed in these examples as silicon structures. By this arrangement, on the one hand, one protects the lipid film 7, and, on the other hand, the adhesion of the microsystem to the active substance reservoir is substantially simplified. Furthermore the electrodes 3 can be manufactured on both sides of the lipid film 7, whereby the electrical field lines in the lipid film can be optimized.

For the manufacture of such a structure, a silicon structure is prepared with a layout, as shown in Figures 5b and 6b. Figure 5b here shows a substrate 16 onto which the electrodes 3 are symmetrically attached, and the microgap 5 is etched in. Furthermore, the integrated electronic system 2 can be seen in this layout view.

The manufacture of such a structure can be carried out with a method as already explained in connection with Figure 3. After the manufacture of this structure, the structure is folded along the broken line shown, so that the corresponding microchannels 5 assume a position one above the other. Thereby, a structure with electrodes arranged on both sides of the lipid film can be constructed, as can be seen in the cross-sectional representation in Figure 5a. The two halves of the substrate 16 are held together by means of a chip adhesive 8, after one half has been selectively coated in the described manner with a lipid film 7.

Besides the arrangement with four electrodes 3 in the area of each microgap 5, shown in Figure 5, one can also use, for example, an arrangement as shown in Figure 6. Here, the manufacture of the microsystem is carried out in the same manner as in Figure 5 except that, in each half of the substrate 16, in each case, only one electrode 3 is arranged on each microchannel 5. Using an appropriate arrangement, a structure can be made by folding this substrate where the electrodes which are arranged on both sides of the microchannels in each case occur alternately

on the lipid film 7 (see also Figure 6a). By the arrangement of the electrodes one can produce, in the lipid film 7, a field line pattern which is changed compared to that of the embodiment of Figure 5.

Finally, Figure 7 shows an arrangement of a structure like that of Figures 5 and 6 on the corresponding active substance reservoirs 10. In the embodiment of Figure 7a, the microsystem is glued to a carrier 15 with active substance reservoirs 10. The corresponding microchannels 5 here are located, in each case, above the active substance reservoirs 10.

The active substance reservoir 10 can also be in the form of a polymer film, onto which the microsystem is also preferably glued. The polymer film contains the active substance to be released and it releases the latter at a defined rate through the microchannels 5 (Figure 7b).

As an alternative to the monolithic integrated silicon structures shown in the preceding examples, the film system can also be constructed with other flexible carrier materials, for example, polyimide. The electronic control circuit in this case is manufactured separately as a silicon circuit and it is integrated in hybrid form in the film system.

Parts list

1 Carrier substrate or silicon chip
2 Integrated electronic system
3 Electrodes
4 Receiver
5 Microgaps or microchannels
6 Capacitor
7 Electroporous layer or film
8 Chip adhesive
9 Prosthesis
10 Active substance reservoir
11 Connection for trigger signal
12 Voltage connection
13 Energy storage device
14 Second carrier substrate
15 Carrier with active substance reservoir
16 Substrate
17 Surface area which promotes adhesion of cells
18 Surface area which prevents adhesion of cells

Claims

1. Microsystem for controlling the release of an active substance from an active substance reservoir with

- a thin carrier substrate (1) which consists of a material which is impermeable with respect to the active substance,

and

one or more through openings (5) for the active substance

which presents one or more through openings (5) for the active substance,

- several electrodes (3) arranged in the area of the through openings (5), and

- electronic system (2), integrated in the carrier substrate (1), for controlling the electrodes (3),

characterized in that

the carrier substrate (1) is designed so it is mechanically flexible, and the through openings (5) are designed as microchannels and/or microgaps each having electrodes (3) arranged on both sides and they are covered on one side of the carrier substrate (1) by a layer (7) made of an electroporous material.

2. Microsystem according to Claim 1, characterized in that the microchannels and/or microgaps (5) present an opening width ≤ 10 µm.

3. Microsystem according to Claim 1 or 2, characterized in that the layer (7) made of electroporous material is enclosed between the carrier substrate (1) and an additional substrate (14), which is designed so it is mechanically flexible in the same manner as the carrier substrate (1) and which is provided with microchannels and/or microgaps (5), where the microchannels and/or microgaps (5) of the additional substrate (14) are arranged in such a manner that they are opposite the microchannels or microgaps (5) of the carrier substrate (1).

4. Microsystem according to Claim 3, characterized in that the arrangement of carrier substrate (1) and additional substrate (14) is formed by the folding of a single substrate (16).

5. Microsystem according to Claim 3 or 4, characterized in that, on the additional substrate (14), in each case, electrodes (3) are arranged on both sides of the microchannels and/or microgaps (5).

6. Microsystem according to one of Claims 1-5, characterized in that the electrodes (3) are in contact with the layer (7) made of electroporous material.

7. Microsystem according to one of Claims 1-6, characterized in that the electrodes (3) are integrated in the carrier substrate (1) and optionally the additional substrate (14).

8. Microsystem according to one of Claims 1-7, characterized in that the layer (7) made of electroporous material covers at least some areas of the electrode (7).

9. Microsystem according to one of Claims 1-8, characterized in that the microchannels and/or microgaps (5) are arranged in an array pattern in the carrier substrate (1).

10. Microsystem according to one of Claims 1-9, characterized in that the lower layer (7) made of electroporous material is interrupted in areas between the microchannels and/or microgaps (5) on the carrier substrate (1).

11. Microsystem according to one of Claims 1-10, characterized in that areas of the carrier substrate (1) and optionally of the additional substrate (14) are coated with a biocompatible material.

12. Microsystem according to one of Claims 1-11, characterized in that on the side of the carrier substrate (1), located opposite the electroporous layer (7), areas (17) of the surface between the microchannels and/or microgaps (5) are designed or coated in such a manner that the cells can adhere to them, and surface areas (18) which are immediately adjacent to the microchannels and/or microgaps (5), as well as the internal walls of the microchannels and/or microgaps (5), are designed or coated in such a manner that cell adhesion is prevented.

13. Microsystem according to one of Claims 1-12, characterized in that the carrier substrate (1) and optionally the additional substrate (14) are formed from a thin Si substrate.

14. Microsystem according to one of Claims 1-12, characterized in that the carrier substrate (1) and optionally the additional substrate (14) are formed from a polyimide film.

15. Microsystem according to one of Claims 1-14, characterized in that the carrier substrate (1) and optionally the additional substrate (14) present a thickness ≤ 80 µm.

16. Microsystem according to one of Claims 1-15, characterized in that a biosensor is integrated into the carrier substrate (1) or applied to it, through which the electronic system (2) is triggered.

17. Microsystem according to one of Claims 1-15, characterized in that a program storage device is integrated in the carrier substrate (1) or applied to it, through which the electronic system (2) is triggered.

18. Microsystem according to one of Claims 1-15, characterized in that a receiver antenna (4) for receiving trigger signals is integrated in the carrier substrate (1) or applied to it, and connected to the electronic system (2).

19. Microsystem according to one of Claims 1-18, characterized in that a receiver coil (4) for wireless power supply is integrated in the carrier substrate (1) or applied to it, and connected to the electronic system (2).

20. Microsystem according to one of Claims 1-19, characterized in that an energy storage device (6,13) is integrated in the carrier substrate (1) or applied to it, and connected to the electronic system (2).

21. Implant with a microsystem according to one or more of the preceding claims with active substance reservoirs (10), which are fixed on or in a surface of the implant (9) and which are completely covered by the microsystem which is attached to the implant (9), where the microgaps and/or microchannels (5) in each case are located above the active substance reservoirs (10).

22. Implant according to Claim 21, characterized in that the active substance reservoirs are designed as recesses in the surface of the implant which receive the active substance.

23. Implant according to Claim 21, characterized in that the active substance reservoirs (10) are formed from a solid phase of the active substance which is applied to the surface of the implant (9) or from a material which releases the active substance.

24. Implant according to one of Claims 21-23, characterized in that the implant (9) is a heart catheter or a stent.

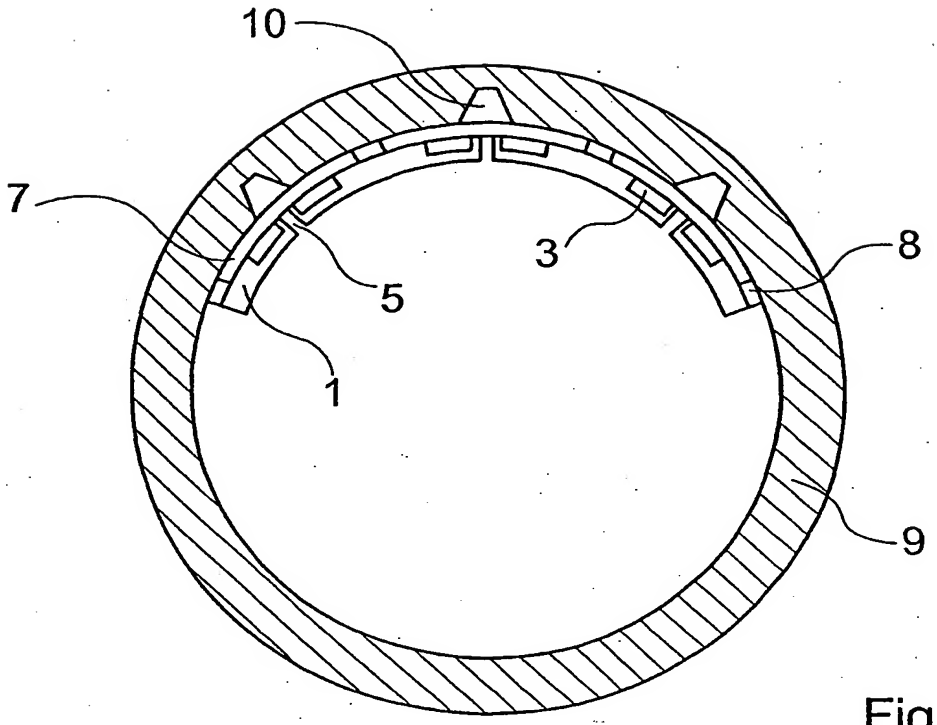

Fig. 1

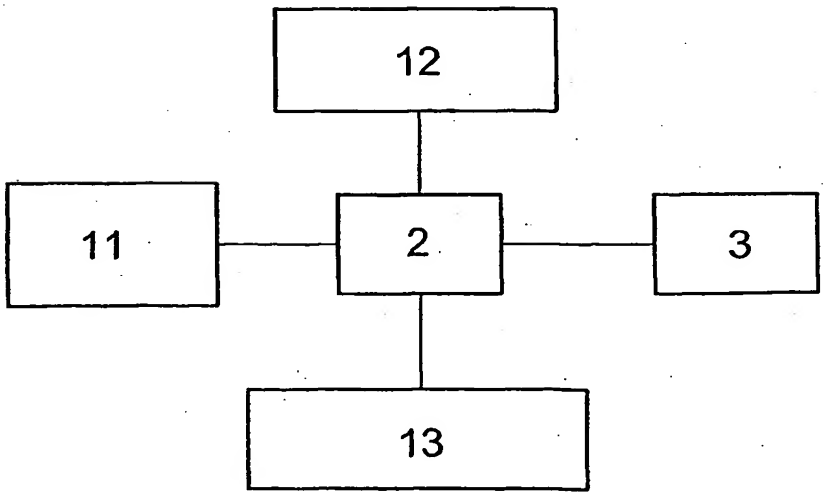

Fig. 2

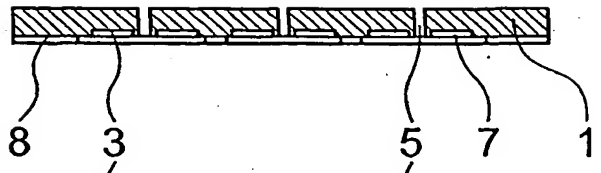

Fig. 3 a

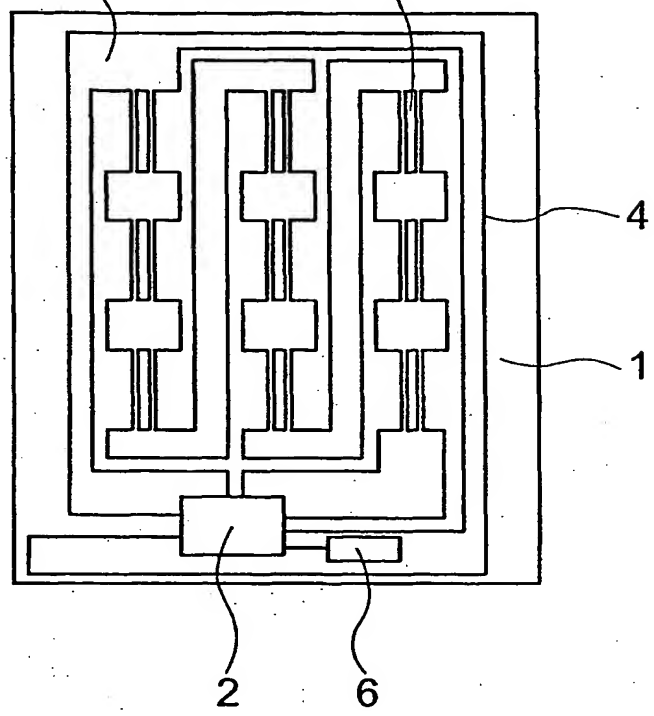

Fig. 3 b

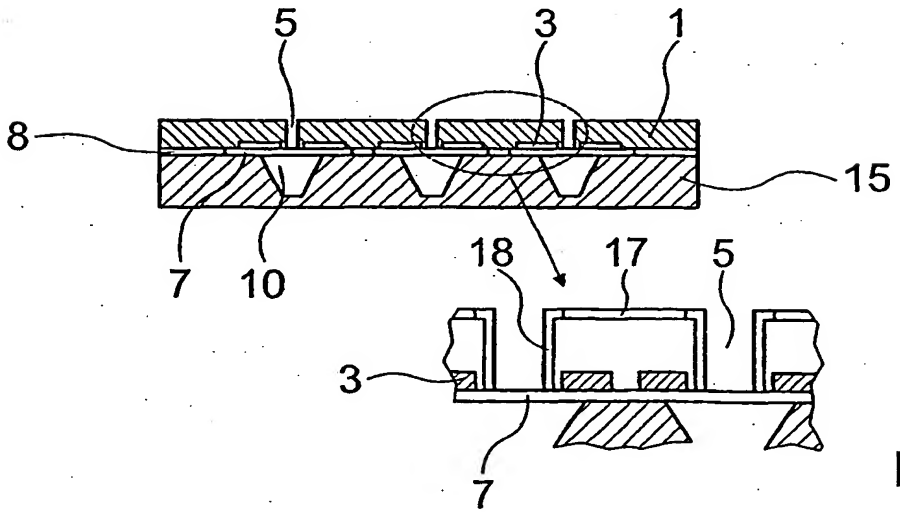

Fig. 4

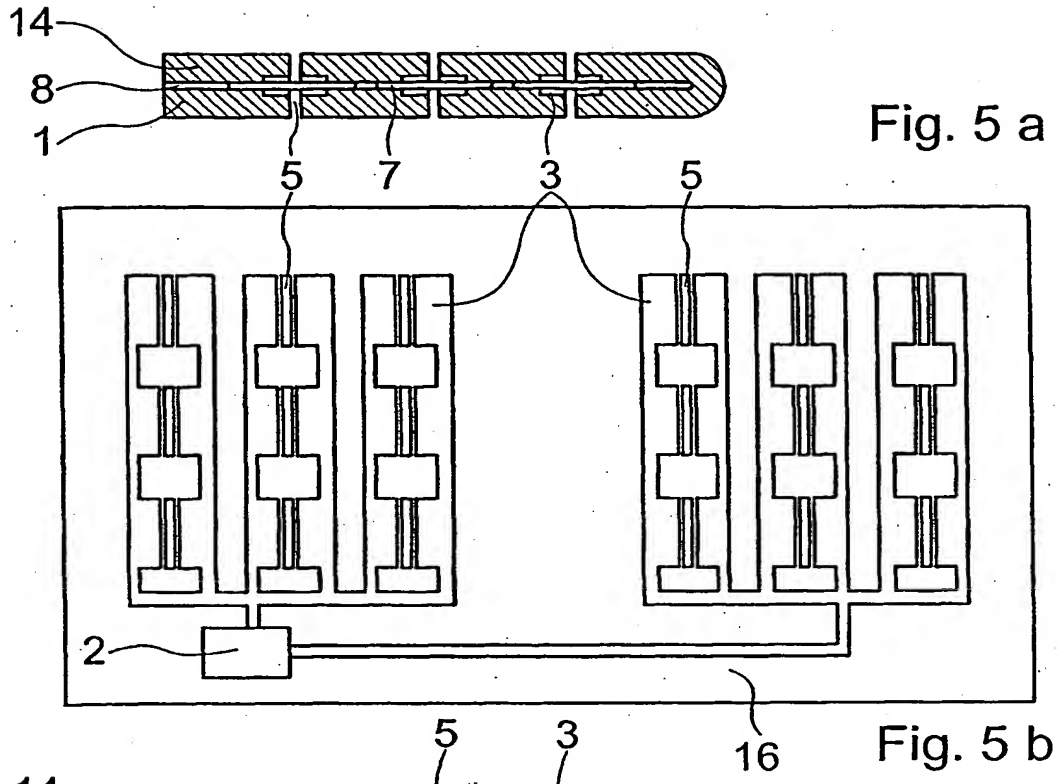

Fig. 5 a

Fig. 5 b

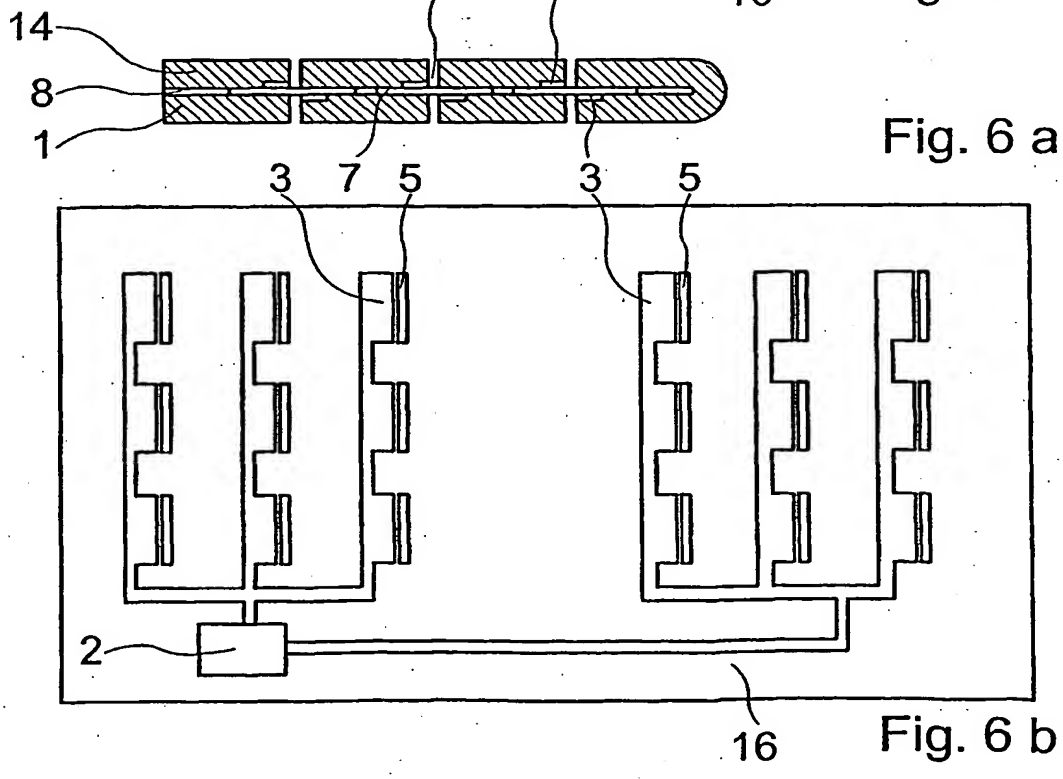

Fig. 6 a

Fig. 6 b

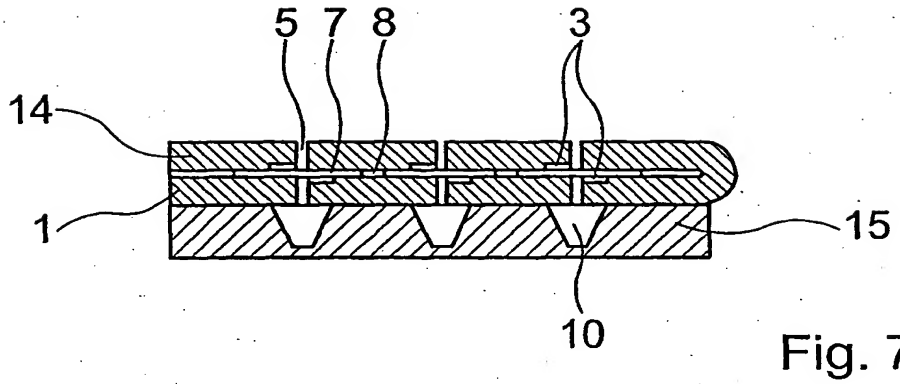

Fig. 7 a

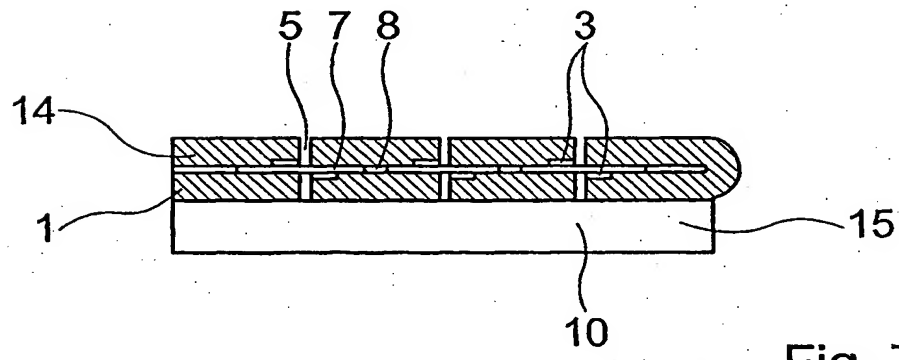

Fig. 7 b